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Entry 1 of 16

File: USPT

Aug 31, 1999

US-PAT-NO: 5944685

DOCUMENT-IDENTIFIER: US 5944685 A

TITLE: Skin-contact type medical treatment apparatus

[Full](#)[Title](#)[Citation](#)[Front](#)[Review](#)[Classification](#)[Date](#)[Reference](#)[Claims](#)[KMC](#)[Image](#)**2. Document ID: US 5843186 A**

Entry 2 of 16

File: USPT

Dec 1, 1998

US-PAT-NO: 5843186

DOCUMENT-IDENTIFIER: US 5843186 A

TITLE: Intraocular lens with antimicrobial activity

[Full](#)[Title](#)[Citation](#)[Front](#)[Review](#)[Classification](#)[Date](#)[Reference](#)[Claims](#)[KMC](#)[Image](#)**3. Document ID: US 5807305 A**

Entry 3 of 16

File: USPT

Sep 15, 1998

US-PAT-NO: 5807305

DOCUMENT-IDENTIFIER: US 5807305 A

TITLE: Iontophoresis device comprising at least one electrode assembly with a reversible composite electrode

[Full](#)[Title](#)[Citation](#)[Front](#)[Review](#)[Classification](#)[Date](#)[Reference](#)[Claims](#)[KMC](#)[Image](#)**4. Document ID: US 5807306 A**

Entry 4 of 16

File: USPT

Sep 15, 1998

US-PAT-NO: 5807306

DOCUMENT-IDENTIFIER: US 5807306 A

TITLE: Polymer matrix drug delivery apparatus

[Full](#)[Title](#)[Citation](#)[Front](#)[Review](#)[Classification](#)[Date](#)[Reference](#)[Claims](#)[KMC](#)[Image](#)**5. Document ID: US 5766144 A**

Entry 5 of 16

File: USPT

Jun 16, 1998

US-PAT-NO: 5766144  
DOCUMENT-IDENTIFIER: US 5766144 A  
TITLE: High efficiency electrode system for iontophoresis

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6. Document ID: US 5498248 A

Entry 6 of 16 File: USPT

Mar 12, 1996

US-PAT-NO: 5498248  
DOCUMENT-IDENTIFIER: US 5498248 A  
TITLE: Iontophoretic structure for medical devices

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Claims](#) | [KOMC](#) | [Image](#)

7. Document ID: US 5362308 A

Entry 7 of 16 File: USPT

Nov 8, 1994

US-PAT-NO: 5362308  
DOCUMENT-IDENTIFIER: US 5362308 A  
TITLE: Disposable dosage unit for iontophoresis-facilitated transdermal delivery, related devices and processes

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Claims](#) | [KOMC](#) | [Image](#)

8. Document ID: US 5766144 A

Entry 8 of 16 File: EPAB

Jun 16, 1998

PUB-NO: US005766144A  
DOCUMENT-IDENTIFIER: US 5766144 A  
TITLE: High efficiency electrode system for iontophoresis

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9. Document ID: WO 9617649 A1

Entry 9 of 16 File: EPAB

Jun 13, 1996

PUB-NO: WO009617649A1  
DOCUMENT-IDENTIFIER: WO 9617649 A1  
TITLE: HIGH EFFICIENCY ELECTRODE SYSTEM FOR IONTOPHORESIS

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Claims](#) | [KOMC](#) | [Clip Img](#) | [Image](#)

10. Document ID: WO 9509670 A1

Entry 10 of 16 File: EPAB

Apr 13, 1995

PUB-NO: WO009509670A1  
DOCUMENT-IDENTIFIER: WO 9509670 A1  
TITLE: DISPOSABLE DOSAGE UNIT FOR IONTOPHORESIS-FACILITATED DELIVERY

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11. Document ID: US 5362308 A

Entry 11 of 16 File: EPAB

Nov 8, 1994

PUB-NO: US005362308A

DOCUMENT-IDENTIFIER: US 5362308 A

TITLE: Disposable dosage unit for iontophoresis-facilitated transdermal delivery, related devices and processes

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12. Document ID: JP 11099209 A

Entry 12 of 16

File: DWPI

Apr 13, 1999

DERWENT-ACC-NO: 1999-295510

DERWENT-WEEK: 199928

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TITLE: Electrode composition for iontophoresis - comprises water soluble polymer layer substance formed between medicine content layer and electrode

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Claims](#) | [KMC](#) | [Image](#)

13. Document ID: DE 3821519 A, EP 348765 A, JP 02098371 A

Entry 13 of 16

File: DWPI

Dec 28, 1989

DERWENT-ACC-NO: 1990-008404

DERWENT-WEEK: 199002

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TITLE: Patches for iontophoretic drug admin. - with flexible conductive polymer electrode layer

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14. Document ID: RD 295020 A

Entry 14 of 16

File: DWPI

Nov 10, 1988

DERWENT-ACC-NO: 1988-366503

DERWENT-WEEK: 198851

COPYRIGHT 2000 DERWENT INFORMATION LTD

TITLE: Drugs via iontophoresis - by incorporating ionic surfactant into polymer drug and applying current to drive charged drug delivery enhancing agents into skin

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15. Document ID: EP 516026 A1, CA 2069650 A, JP 05230313 A, US 5346935 A

Entry 15 of 16

File: DWPI

Dec 2, 1992

DERWENT-ACC-NO: 1992-400415

DERWENT-WEEK: 199249

COPYRIGHT 2000 DERWENT INFORMATION LTD

TITLE: Stable polyvinyl alcohol hydrogel for iontophoretic drug delivery - contains resin or polymer of high water retention capacity to delay evapn., e.g. sodium hyaluronate

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16. Document ID: WO 9115259 A, AU 636744 B, AU 9175884 A, CA 2038968 A, DE 69102699 E, EP 522011 A1, EP 522011 B1, ES 2056646 T3, FI 9204343 A, IE 64973 B, JP 05505955 W, NO 9203591 A, NZ 237560 A, PT 97140 A, US 5084006 A, US 5162043 A, US 5326341 A, ZA 9102227

A.

Entry 16 of 16

File: DWPI

Oct 17, 1991

DERWENT-ACC-NO: 1991-324986

DERWENT-WEEK: 199744

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TITLE: Iontophoretic delivery device - with hydrophobic polymer component in agent or electrolyte reservoir to prevent delamination

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Terms	Documents
iontophoresis adj5 (polymer or polymers)	16

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## Document Number 12

Entry 12 of 16

File: DWPI

Apr 13, 1999

DERWENT-ACC-NO: 1999-295510

COPYRIGHT 2000 DERWENT INFORMATION LTD

TITLE: Electrode composition for iontophoresis - comprises water soluble  
polymer layer substance formed between medicine content layer and  
electrode

TTX:

ELECTRODE COMPOSITION IONTOPHORESIS COMPRISE WATER SOLUBLE POLYMER LAYER  
SUBSTANCE FORMING MEDICINE CONTENT LAYER ELECTRODE[Main Menu](#) [Search Form](#) [Result Set](#) [Show S Numbers](#) [Edit S Numbers](#)[First Hit](#)[Previous Document](#)[Next Document](#)[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Claims](#) [KWIC](#)[Help](#) [Logout](#)

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## Document Number 11

Entry 11 of 16

File: EPAB

Nov 8, 1994

DOCUMENT-IDENTIFIER: US 5362308 A

TITLE: Disposable dosage unit for iontophoresis-facilitated transdermal delivery, related devices and processes

## FPAR:

Provided are disposable dosage units for use in iontophoresis-facilitated transdermal delivery which have hydrophilic polymer first and second layers, the first layer having ionic resin particles dispersed therein and the second layer having an ionized pharmaceutical contained. The second layer having on its surface a thin fabric layer bearing an adhesive layer. The polymer first and second layers are separated by a permselective membrane. Also provided are related devices and processes using the novel disposable dosage units.

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## Document Number 6

Entry 6 of 16

File: USPT

Mar 12, 1996

DOCUMENT-IDENTIFIER: US 5498248 A

TITLE: Iontophoretic structure for medical devices

CLPR:

11. The iontophoresis catheter of claim 7, wherein said conductive polymer is chosen from the group consisting of polyvinyl, polyurethane, polyester, polyethylene, and polyvinylidene.

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## Document Number 4

Entry 4 of 16

File: USPT

Sep 15, 1998

DOCUMENT-IDENTIFIER: US 5807306 A

TITLE: Polymer matrix drug delivery apparatus

## DEPR:

For iontophoresis techniques to be used, the drug within the polymer matrix 12 should have specific characteristics. Ideally, the drug should have an ionic nature or have other ionic molecules bound to the active components of the drug to promote the iontophoretic movement or transport from the polymer matrix 12. An electrical current for the iontophoretic process of FIG. 2 is produced between the electrodes 18 and 20 by an external power source 30 through the electrical leads 22 and 24, respectively.

## DEPR:

The embodiment in FIG. 11 preferably utilizes iontophoresis to drive the drug from the polymer matrix 124. Iontophoresis is preferred because it facilitates both transport of a drug and enhances tissue penetration. If iontophoresis is used, then similarly to the structure shown in FIG. 2, the catheter electrode 128 is located within the polymer matrix 124, while the other electrode (not shown) is preferably located on the body of the patient.

## DEPR:

In the case of the vascular delivery embodiments (FIGS. 1-9), the tissue delivery embodiment (FIG. 11), and the erectile dysfunction embodiment (FIGS. 14-17), described above, phonophoresis (sometimes referred to as sonophoresis) can be used as an alternative to iontophoresis to transport drugs from the polymer matrix into the surrounding tissue.

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## Document Number 7

Entry 7 of 125

File: USPT

Mar 23, 1999

DOCUMENT-IDENTIFIER: US 5885616 A  
TITLE: Sustained release drug delivery system suitable for oral administration

## BSPR:

Upon exposure of the drug delivery system to higher pHs, a pH sensitive polymer in the second polymer layer can dissolve. The dissolution of the pH sensitive polymer disrupts the polymer film and facilitates the complete release of the active agent from the second drug compartment. In turn, the first polymer compartment becomes exposed to the surrounding medium.

## CLPR:

19. The drug delivery system of claim 1, wherein said first polymer compartment, or second polymer compartment, or both first and second polymer compartments, contains one or more pH sensitive polymer(s) selected from the group consisting of hydroxypropyl methylcellulose phthalate, cellulose acetate phthalate, other cellulose ethers or esters, and acrylic resins.

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## Document Number 12

Entry 12 of 125

File: USPT

Nov 24, 1998

DOCUMENT-IDENTIFIER: US 5840338 A

TITLE: Loading of biologically active solutes into polymer gels

## DEPR:

3. One would like to develop a pH-sensitive polymer gel suitable for use in agricultural controlled release. Cellulose ethers (i.e., hydroxypropylcellulose-HPC) are suitable as polymer backbones since they have a KATP when used for food additives (Aqualon Product Data, *supra*). Cellulose ethers may be crosslinked with adipic acid and both HPC and adipic acid have KATP's for use as food additives (see above), thus satisfying pathway 1. Surfactants such as diethanolamide condensates, n-alkyl (2-C<sub>8</sub>-C<sub>18</sub>) amine acetates, and di-n-alkyl (C<sub>8</sub>-C<sub>18</sub>) dimethyl ammonium chloride (21 C.F.R. 172.710), suitable for use with pesticides, may be added to the gel, satisfying Pathway 2 that starting materials may be used in processes for making other KATP materials.

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## Document Number 15

Entry 15 of 125

File: USPT

Aug 4, 1998

DOCUMENT-IDENTIFIER: US 5788687 A

TITLE: Compositions and devices for controlled release of active ingredients

## ABPL:

A method for the controlled release of a biologically active agent wherein the agent is released from a hydrophobic, pH-sensitive polymer matrix is disclosed and claimed. In one embodiment, the polymer matrix swells when the environment reaches pH 8.5, releasing the active agent. A polymer of hydrophobic and weakly acidic comonomers is disclosed for use in the controlled release system. In another embodiment, weakly basic comonomers are used and the active agent is released as the pH drops. Further disclosed is a specific embodiment in which the controlled release system may be used. The pH-sensitive polymer is coated onto a latex catheter used in ureteral catheterization. A common problem with catheterized patients is the infection of the urinary tract with urease-producing bacteria. In addition to the irritation caused by the presence of the bacteria, urease produced by these bacteria degrade urea in the urine, forming carbon dioxide and ammonia. The ammonia causes an increase in the pH of the urine. Minerals in the urine begin to precipitate at this high pH, forming encrustations which complicate the functioning of the catheter. A ureteral catheter coated with a pH-sensitive polymer having an antibiotic or urease inhibitor trapped within its matrix releases the active agent when exposed to the high pH urine as the polymer gel swells. Such release can be made slow enough so that the drug remains at significant levels for a clinically useful period of time. Other uses for the methods and devices of this invention include use in gastrointestinal tubes, respiratory trap lines and ventilation tubes, dye releasing pH sensitive sutures, active agent release from contact lenses, penile implants, heart pacemakers, neural shunts, food wraps, and clean room walls.

## BSPR:

The subject invention concerns a method for the controlled release of an agent from a pH sensitive polymer. The agent is released from the matrix of a polymer gel when the pH of the surrounding environment reaches a desired level. This method of controlled release can be used to ensure that the agent is delivered to a specific area and delivered only when the need for the agent arises. Methods such as these are also sometimes called stimulated, regulated, or triggered release.

## BSPR:

To adjust the flexibility of the coating, various combinations of monomer can be used, or the active composition (pH sensitive polymer plus antibiotic) can be formed into microspheres and incorporated into an elastomeric matrix in the same way that a filler, such as SiO<sub>2</sub> sub.2, is currently used in an elastomer such as silicone.

## DEPR:

Release of an antibiotic when bacterial surface growth is present, but not at other times, advantageously controls bacterial growth without the excessive release of antibiotics. A specific embodiment of the subject

invention concerns a pH responsive polymer or hydrogel which is useful for the pH stimulated release of an antibiotic into infected urine. Bacterial presence is detected by sensing a pH change induced by the urease-producing organism which causes the release of basic ammonia into the urine. High pH causes minerals in the urine to precipitate, forming encrustations. A pH-sensitive polymer such as a weak carboxylic acid can be used so that when the pH increases, ionization occurs and the polymer becomes swollen, causing antibiotic to be released which kills the urease-producing bacteria. Control of these bacteria helps regulate urine pH.

## DEPR:

In another industrial application of this invention, the pH sensitive polymer matrix of this invention is used as a food-wrap, such that if the food, for example meat, becomes contaminated by bacterial infection, the wrap will release a dye or other indicator as the pH increases or decreases beyond a pre-set limit. In this way, spoiled food will not be consumed. In addition, a dye could be released from microspheres, intermixed with food, e.g. ground meat. The dye releasing polymer may be an interpenetrating network or a coating.

## DEPR:

In another application, for example where the walls of a clean room, spacecraft, or space station must be free of bacterial contamination, the walls may be coated with the pH sensitive polymer matrix and an indicator or sterilant released should bacterial contamination of the walls occur. Likewise, sterilants or pH buffers could be released from the walls or bottom of a swimming pool or from a free floating container as the pH drops or rises beyond a pre-determined limit.

## CLPR:

1. A medical device for controlling a bacterial infection which causes a change in the pH of the environment of the device, wherein said device comprises a pH-sensitive polymer matrix containing a biologically active agent, said agent being a bacterial control agent or an antibacterial agent, said agent further being released from said polymer matrix upon said change of pH, wherein said device is selected from the group consisting of sutures, contact lenses, catheters, indwelling stents, shunts or tubes, gastrointestinal tubes, respiratory tubes, penile implants, heart pacemakers, and neural shunts.

## CLPR:

3. A medical device for controlling a bacterial infection which causes a change in the pH of the environment of the device, wherein said device comprises a pH-sensitive polymer matrix containing a biologically active agent, said agent being a bacterial control agent or an antibacterial agent, said agent further being released from said polymer matrix upon said change of pH, wherein said pH-sensitive polymer matrix containing said biologically active agent is fabricated by folding an interpenetrating network comprising both plastic or elastomeric polymer and a pH sensitive polymer formed in situ from monomers soaked into said plastic or elastomeric polymer.

## CLPR:

6. A medical device for controlling a bacterial infection which causes a change in the pH of the environment of the device, wherein said device comprises a pH-sensitive polymer matrix containing a biologically active agent, said agent being a bacterial control agent or an antibacterial agent, said agent further being released from said polymer matrix upon said change of pH, wherein said pH-sensitive polymer matrix containing said biologically active agent is fabricated by polymerizing acrylamide monomers on the surface of oxidized natural latex rubber to form a polyacrylamide coating on said oxidized latex rubber, and then hydrolyzing the polyacrylamide to form a polyacrylic acid coating.

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## Document Number 17

Entry 17 of 125

File: USPT

Jun 16, 1998

DOCUMENT-IDENTIFIER: US 5766580 A

TITLE: Controlled release of miotic and mydriatic drugs in the anterior chamber

## DEPR:

Soluble microcapsules may be derived from inherently biodegradable polymers, such as poly-DL-lactide or poly-DL-lactide-co-glycolide, which, in dry form, may be made into microcapsules containing an appropriate agent (Clarke et al., 1994, *Polymer Preprints* 35(2):73). Alternatively, soluble microcapsules may be derived from pH sensitive polymers, where a change in pH can cause expansion of the microcapsule, leading to a sustained release drug delivery system. An example of such a pH-sensitive polymer is poly(L)-lysine-alt-terephthalic acid, which, at pH values greater than 6, expands (Makino et al., 1994, *Polymer Preprints* 35: 54). Biodegradable microcapsules containing miotic or mydriatic agent may be prepared using polymers, such as polylactide or polylactide-co-glycolide, that decompose after a period of time.

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## Document Number 22

Entry 22 of 125

File: USPT

Apr 21, 1998

DOCUMENT-IDENTIFIER: US 5741506 A

TITLE: Use of active ingredients protected against degradation in the rumen as hepatoprotectors

## CLPR:

1. A method for the prevention or treatment of hepatic steatosis in ruminants, said method comprising administering to a ruminant in an amount effective to prevent or treat hepatic steatosis a composition containing at least one active ingredient, said at least one active ingredient being selected from amino acids, polyols, amino alcohols, and vitamins, and said at least one active ingredient being protected from degradation in the rumen by a composition comprising a pH-sensitive polymer and a fatty substance or a composition stable in the rumen and subject to enzymatic degradation in the abomasum or small intestine.

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## Document Number 33

Entry 33 of 125

File: USPT

Mar 11, 1997

DOCUMENT-IDENTIFIER: US 5609590 A  
TITLE: PH-triggered osmotic bursting delivery devices

## DEPR:

Preferred devices include those described in Examples 12, 13, and 14 described generally below. Particularly preferred capsules include those having a semipermeable membrane of ethylene vinyl alcohol, cellulose acetate or ethylcellulose surrounding the beneficial agent and containing an aqueous swellable material such as sodium carboxymethylcellulose in the core. The capsule halves are sealed together with a pH-sensitive adhesive consisting of a mixture of polymethylmethacrylate and acrylic acid/acrylic ester copolymer, preferably about 5 to 50 wt % polymethylmethacrylate and 50 to 75 wt % acrylic acid/acrylic ester copolymer and particularly about 15 to 25 wt % polymethylmethacrylate and 75 to 85 wt % acrylic acid/acrylic ester copolymer. Sufficient pH-sensitive polymer is used to provide a seal thickness of 20 .mu.m to 100 .mu.m.

## DEPR:

Particularly preferred tablets include those having a core of beneficial agent, osmagent (preferably lactose), and aqueous swellable material (preferably sodium carboxymethylcellulose). The tablets have a semipermeable membrane of cellulose acetate which is preferably about 20 to 100 .mu.m thick. The semipermeable membrane is surrounded by a pH-sensitive coating made of cellulose acetate phthalate coating blended with from 0 to 75 wt % cellulose acetate, preferably about 5 to 75 wt % cellulose acetate and 25 to 95 wt % cellulose acetate phthalate and particularly about 25 to 35 wt % cellulose acetate and 65 to 75 wt % cellulose acetate phthalate. Sufficient pH-sensitive polymer is used to provide a thickness of 20 .mu.m to 150 .mu.m.

## DEPR:

Particularly preferred multiparticulate beads are those having the same cores as are described for the tablets (above). Likewise the beads have a cellulose acetate semipermeable coating which is preferably about 15 to 50 .mu.m thick. The semipermeable membrane is coated with a pH-sensitive coating made of cellulose acetate phthalate blended with from 0 to 75 wt % cellulose acetate, preferably, about 5 to 75 wt % cellulose acetate and 25 to 95 wt % cellulose acetate phthalate and particularly about 40 to 60 wt % cellulose acetate and 40 to 60 wt % cellulose acetate phthalate. Preferably, sufficient pH-sensitive polymer is used to provide a thickness of 15 .mu.m to 120 .mu.m.

## DEPR:

PH-triggered polymer solutions were prepared by mixing pH-sensitive polymers with nondissolving materials. The pH-sensitive polymer tested was Eudragit S-100 (Rohm Pharma.). The nondissolving polymers tested were Eudragit RL (Robin Pharma) and polymethyl methacrylate PMMA V920 (Rohm Haas). Films were made of these materials by dissolving them in acetone, casting the solution on a glass plate, and then allowing the acetone to evaporate. The trigger-pH is believed to range from 4.5 to 7 for all of the films described in this example.

## DEPR:

Results from these tests with polymer films indicate that the break time and corresponding delivery site can be controlled by the ratio of pH-sensitive polymer to nondissolving polymer.

## DEPR:

Pseudoephedrine tablets made by standard direct-compression techniques as described in Example 11 and coated with a CA 398-3 semipermeable coating were coated with pH-triggered coating solutions of cellulose acetate 398-10 (Eastman Chemical Products, Inc.) and cellulose acetate phthalate CD-910 (FMC Corp.) dissolved in acetone where the ratio of pH-sensitive polymer to nondissolving material varied. The tablets were coated with the pH-triggered coating solutions as described in Example 1.

## DEPR:

Burst times were determined from these tablets by running release-rate tests in gastric and intestinal buffers as described in Example 8. The burst times for tablets with varying ratios of pH-sensitive polymer is shown in FIG. 12. Burst times decrease as the content of pH-sensitive material in the coating increases. In FIG. 12, burst time in hours (Y) is graphed against % cellulose acetate phthalate content (X).

## DEPR:

Example 12 demonstrates that the burst time and corresponding intestinal delivery site can be controlled by the ratio of pH-sensitive polymer to nondissolving material in the pH-triggered coat.

## DEPR:

Capsules were made with pH-triggered membrane seals as described in Example 4. Seal solutions were made where the ratio of pH-sensitive polymer (Eudragit S-100, Rohm Pharma.) to nondissolving material (polymethyl methacrylate, PMMA V-920, Rohm Haas) was varied.

## DEPR:

Release-rate tests were conducted as described in Example 9 to determine the capsule burst times. The burst times for the pH-triggered membrane sealed capsules with varying ratios of pH-sensitive polymer are shown in FIG. 13. FIG. 13 graphs burst time in intestinal buffer in hours (Y) against weight % of PMMA V920 in capsule seals (X).

## DEPR:

Example 13 demonstrates that the burst time and corresponding intestinal delivery site can be controlled by the ratio of pH-sensitive polymer to nondissolving material in the pH-triggered capsule seal.

## DEPR:

Pseudoephedrine tablets made by standard direct-compression techniques and coated with a CA 398-3 semipermeable coating as described in Example 11 were coated with pH-triggered coating solutions of cellulose acetate 398-10 (Eastman Chemical Products, Inc.) and cellulose acetate phthalate CD-910 (FMC Corp.) dissolved in acetone where both the coating thickness and the ratio of pH-sensitive polymer to nondissolving material was varied. The tablets were coated with the pH-triggered coating solutions as described in Example 1.

## DEPR:

Burst times were determined from these tablets by running release rate tests into gastric and intestinal buffers as described in Example 8. The burst times for tablets with varying thickness and ratio of pH-sensitive polymer is shown in FIG. 14. FIG. 14 graphs burst time in hours (Y) vs. weight % cellulose acetate phthalate (X) vs. coating thickness in .mu.m (Z).

## DEPR:

Example 14 demonstrates that the burst time and corresponding intestine site of delivery can be controlled by both the coating thickness and the ratio of pH-sensitive polymer to nondissolving material in the

pH-triggered coat.

DEPR:

Both the tablets in gastric buffer and intestinal buffer begin releasing drug after the same amount of water was imbibed, but the release mechanism was entirely different. The tablets which had degraded due to the pH of the intestinal buffer burst, whereas the tablets whose coating was unaffected just leaked. This is because the burst time and bursting mechanism are determined by both the change in permeability and the change in coating strength due to degradation of the pH-sensitive polymer in the coating.

DEPC:

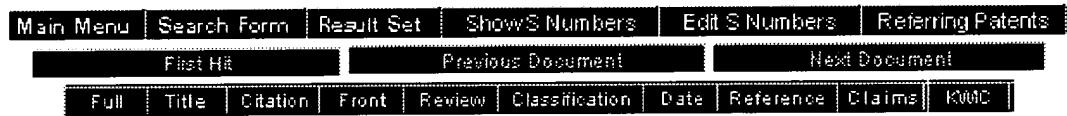
TABLET BURST TIME CAN BE CONTROLLED BY THE RATIO OF PH-SENSITIVE POLYMER TO NONDISSOLVING MATERIAL IN THE PH-TRIGGERED MEMBRANE COATING

DEPC:

CAPSULE BURST TIME CAN BE CONTROLLED BY THE RATIO OF PH-SENSITIVE POLYMER TO NONDISSOLVING MATERIAL IN THE PH-TRIGGERED MEMBRANE SEAL

DEPC:

TABLET BURST TIME CAN BE CONTROLLED BY BOTH THE COATING THICKNESS AND THE RATIO OF PH-SENSITIVE POLYMER TO NONDISSOLVING MATERIAL IN THE PH-TRIGGERED MEMBRANE COATING



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## Document Number 4

Entry 4 of 5

File: DWPI

Nov 4, 1999

DERWENT-ACC-NO: 2000-013418

COPYRIGHT 2000 DERWENT INFORMATION LTD

TITLE: New polyanionic polymers, allow control of fusogenicity and/or permeability of liposomes by change in pH of environment

## ABTX:

DETAILED DESCRIPTION - Polyanionic polymers are of formula (I): R1, R3 = H, OH, amino, optionally substituted alkyl or ligand; Y = H or optionally substituted alkyl, cycloalkyl, aryl or heteroaryl; X = optionally substituted amino, O, S or C single bond; R2 = H, alkyl, alkenyl, dialk(en)ylglycerolyl, diacylglycerolyl, 1,2-diacyl-sn-glycero-3-phospho- thylene, 1,2-dialkoxy-3-aminopropanyl or 1,2-diacyloxy-3-aminopropanyl; and n, i = greater than 1. An INDEPENDENT CLAIM is also included for pH-sensitive liposomes comprising lipid and (I).

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## Document Number 5

Entry 5 of 5

File: DWPI

Aug 6, 1998

DERWENT-ACC-NO: 1998-437175

COPYRIGHT 2000 DERWENT INFORMATION LTD

TITLE: Improved vaccine for treating cancer, infectious disease and auto-immune disease - comprises encapsulated antigen and immuno-modulator, and uses pH-sensitive liposome(s)

## ABTX:

The carrier is a virosome, a pH-sensitive liposome or a liposome containing lipophylic polylysine, which is encapsulates the antigen and at least 1 IMM. The carrier is a chloroform-free pH-sensitive liposome comprising DOPE (dioleoylphosphatidyl ethanolamine) and CHEMS (cholesteryl hemisuccinate) which are formed at a pH of 8.5-9.5. The liposomes are formed at the highest concentration of lipid possible, to maximise the amount of antigens and IMMs that can be encapsulated. The carrier may be a particulate bead made of glass, iron, biodegradable polymer, or other material.

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## Document Number 2

Entry 2 of 5

File: USPT

Jun 22, 1999

DOCUMENT-IDENTIFIER: US 5914126 A  
TITLE: Methods to deliver macromolecules to hair follicles

## DEPR:

In another embodiment, the invention comprises a liposome composition comprising one or more phospholipids selected from the group consisting of PC, EPC, DOPC, DPPC, PE, DOPE and cholesterol, combined with one or more phospholipids to form pH-sensitive liposomes. pH-sensitive liposomes are generally well known and their preparation has been described by Straubinger et al., FEBS Letts. 179:148-154, 1985. A preferred pH sensitive liposome comprises oleic acid (OA) and PE at a molar ratio of 3:7. OA is available from a variety of commercial sources, including Sigma (St. Louis, Mo.). Several pH-sensitive liposome systems have been described. There are two main categories: intrinsically pH-sensitive liposomes and those which utilize an external non-lipid trigger. Intrinsically pH-sensitive liposomes are constructed by combining phosphatidylethanolamine (PE) with one of a number of acidic amphiphiles. Externally triggered pH-sensitive liposomes combine an otherwise stable liposome with an external soluble component such as a titratable polymer or a titratable synthetic peptide which undergoes a conformational change upon acidification. To increase the efficacy of intracellular delivery, liposomes can be made pH-sensitive and able to fuse with cellular membrane at decreased pH values (pH drop from 7.4 to 6.5) or in the presence of polyethylene glycol. Some pH-sensitive liposomes are composed of DOPE: Cholesterol hemisuccinate at molar ratios 2:1.

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Entry 1 of 5

File: USPT

Oct 12, 1999

US-PAT-NO: 5965157

DOCUMENT-IDENTIFIER: US 5965157 A

TITLE: Method to provide for production of hair coloring pigments in hair follicles

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Claims](#) [KMC](#) [Image](#)**2. Document ID: US 5914126 A**

Entry 2 of 5

File: USPT

Jun 22, 1999

US-PAT-NO: 5914126

DOCUMENT-IDENTIFIER: US 5914126 A

TITLE: Methods to deliver macromolecules to hair follicles

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Claims](#) [KMC](#) [Image](#)**3. Document ID: US 5753263 A**

Entry 3 of 5

File: USPT

May 19, 1998

US-PAT-NO: 5753263

DOCUMENT-IDENTIFIER: US 5753263 A

TITLE: Method to deliver compositions conferring resistance to alopecia to hair follicles

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Claims](#) [KMC](#) [Image](#)**4. Document ID: WO 9955743 A1**

Entry 4 of 5

File: DWPI

Nov 4, 1999

DERWENT-ACC-NO: 2000-013418

DERWENT-WEEK: 200001

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TITLE: New polyanionic polymers, allow control of fusogenicity and/or permeability of liposomes by change in pH of environment

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Claims](#) [KMC](#) [Image](#)**5. Document ID: WO 9833520 A1**

Entry 5 of 5

File: DWPI

Aug 6, 1998

DERWENT-ACC-NO: 1998-437175

DERWENT-WEEK: 199837

COPYRIGHT 2000 DERWENT INFORMATION LTD

TITLE: Improved vaccine for treating cancer, infectious disease and auto-immune disease - comprises encapsulated antigen and immuno-modulator, and uses pH-sensitive liposome(s)

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